Remarks:

Applicant has carefully studied the final Examiner's Action mailed June 5, 2009. Applicant thanks the Examiner for their careful attention in reviewing the application. The amendments appearing above and these explanatory remarks are believed to be fully responsive to the Action. Accordingly, this important patent application is now believed to be in condition for allowance.

Status of the Claims

Claims 1-2, 4, 7, 10, 12-17, 19, and 20-30 were pending in the Office Action mailed June 5, 2009. Claims 1, 7, 10, 13, 14, 15, 17, 20 and 23 have been amended. Support for the amended claims can be found in the original specification and figures. Claim 21 has been canceled. No new matter has been added. Therefore, claims 1-2, 4, 7, 10, 12-17, 19, 20 and 22-30 are currently pending and under examination.

Claim Rejections – 35 U.S.C. §103(a)

The applicant acknowledges the recitation of 35 U.S.C. §103(a).

Weiss in view of Sanberg and Grabowski:

Claims 1, 2, 4, and 17 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent 5,851,832 to Weiss (hereinafter "Weiss") in view of Sanberg et al. (1997. Soc. Neurosci Abstr 23(1-2):346, abstract 140.9) and Grabowski et al. (1994. Exp Neural. 127(1):126-136). Applicant respectfully traverses this rejection on the grounds that one or more elements are missing from the cited combination;

Weiss fails to teach the administration of about 6 million hNT neuronal cells and Sanberg and Grabowski fail to resolve that deficiency

Office rejects claims 1, 2, 4, and 17 under 35 U.S.C. § 103(a) as being unpatentable under Weiss in view of Sanberg and Grabowski. Amended claim 1 is directed to "[a] method of treating stroke in a human who has undergone a stroke at least three hours earlier, said method

comprising delivering about 6 million viable hNT neuronal cells to a plurality of brain area sites involved in the stroke." Office asserts on page 2 of the Office Action dated June 5, 2009 that Weiss teaches methods of treating diseases, including stroke, by the administration of the progeny of *human* neural stem cells. (emphasis added) Weiss does not teach the administration of human neural stem cells as claimed by Office but rather teaches the administration of mice neural stem cells.

Office uses the teachings of Sanberg to overcome the shortcomings of Weiss with respect to the use of hNT cells. Sanberg states that administration of between 20,000 and 40,000 hNT cells, with 40,000 cells being the optimal dose, is effective to restore behavioral functions in ischemic rats. According to Office this dose is equal to the administration of 10 million cells to a human. Applicant has amended claim 1 to disclose the administration of about 6 million cells. The administration of 10 million cells is nearly double the amount that is disclosed in amended claim 1 and as such cannot be said to be equal to about 6 million cells.

In conclusion, the cited combination fails to teach the administration of about 6 million hNT cells for treatment of stroke and as such cannot be said to obviate the present invention.

Weiss fails to teach waiting at least 3 hours before delivering treatment and Sanberg and Grabowski fail to resolve that deficiency

One of the elements of amended claim 1 is to delay delivery of the hNT neurons until at least 3 hours post-stroke. Neither Sanberg nor Weiss teaches waiting at least 3 hours post-stroke for delivery of cells nor mentions delaying delivery of the cells for any time period. Grabowski expressly teaches waiting at least 5-7 days after the lesion occurs before doing graft implantation and in fact teaches away from waiting for any time period shorter than 5 days. Grabowski cites specific results that indicate delivering treatment prior to 5 days post-stroke was unsuccessful in their studies. Since Grabowski fails to teach waiting for time periods less than 5 days and in fact teaches against delaying treatment for time periods of less than 5 days, it does not resolve the deficiencies of Weiss and Sanberg. The cited combination fails to teach each and every element of the claims in question and consequently cannot be said to render the present invention obvious.

Weiss fails to teach waiting at least 3 months post-stroke before administering treatment and Sanberg and Grabowski fail to resolve that deficiency

Claim 4 is directed to "the method of claim 1 wherein the stroke has taken place at least 3 months earlier." As stated above, both Weiss and Sanford fail to teach any delay in treatment. Office uses the Grabowski reference to provide the element of delay in treatment, however as noted by Office on page 3 of the Office Action dated June 5, 2009, Grabowski does not teach waiting at least 3 months before administering treatment as indicated in claim 4 of the present application. Grabowski teaches waiting at least 5-7 days after the lesion occurs before doing graft implantation and places an upper limit on the delay period by stating that previous studies have found that a delay of 30-60 days after lesion was unsuccessful. These limits proposed in Grabowski, when taken together, propose a range of delay of 5-60 days before administering treatment. Clearly the 3 month (90 day) delay that is indicated in claim 4 falls outside of the range taught in Grabowski. Given that Weiss, in view of Sanberg and Grabowski, fail to teach the element of delaying treatment for at least 3 months, the combination of references fails to teach each and every element of the claims in question to yield the present invention and thus a finding of obviousness cannot be found.

In conclusion, for the foregoing reasons, Weiss in view of Sanberg and Grabowski fails to teach each and every element of the claims in question and thus fail to obviate the present invention. It is therefore respectfully requested that the rejection of claims 1, 2, 4, and 17 under 35 U.S.C. § 103(a) be withdrawn.

Sanberg in view of Weiss and Uchida:

Claims 7, 10, 12-17 and 19 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Sanberg et al. (1996. Soc. Neurosci. Abstr. 22(1-3):578, abstract 232.9) in view of U.S. Patent 5,851,832 to Weiss et al. (hereinafter "Weiss") and Uchida et al. (1995. Exp. Neurol 132:194-208). Applicant respectfully traverses this rejection on the grounds that one or more elements are missing from the cited combination.

Applicant submits that the rejection under 35 U.S.C. § 103(a) is improper for reasons of record as presented above with respect to the rejection of claims 1, 2, 4, and 17 over the Weiss patent in view of Sanberg and Grabowski.

Sanberg fails to teach administration of about 6 million hNT cells to a plurality of brain sites in a human and Weiss and Uchida fail to resolve that deficiency

Amended claims 7, 10, 13, and 17 of the present application all recite administration of about 6 million hNT cells to a plurality of brain sites. In contrast, as stated above with respect to the rejection of claims 1, 2, 4, and 17 over Weiss in view of Sanberg and Grabowski, while Sanberg teaches the administration of hNT cells, it does not teach the administration of about 6 million cells to a human who has undergone stroke nor does it teach the administration to a plurality of brain sites. Weiss and Uchida similarly do not teach the administration of about 6 million hNT cells to a human at a plurality of brain sites. Given that none of the references teach the administration of about 6 million cells to a plurality of brain sites in a human as well as for the reasons outlined above in response to the rejection of claims 1, 2, 4, and 17 over Weiss in view of Sanberg and Grabowski, the cited combination of references fails to teach all of the elements of the claims in question and thus there is no basis for a legal finding of obviousness. Claim 12 is dependent upon claim 10 and is allowable as a matter of law upon the allowance of claim 10. Applicant therefore respectfully requests that the rejection of claims 7, 10, 12, 13, and 17 be withdrawn.

Sanberg fails to teach the administration of about 6 million hNT cells to a plurality of sites in the central nervous system or the cerebral spinal fluid and Weiss and Uchida fail to resolve that deficiency

Claim 14 is directed to, "[a] method of improving sensory function in a person who has experienced stroke-induced brain damage which interferes with sensation, said method comprising delivering a sterile composition of at least 6 million hNT neuronal cells to a plurality of sites of the central nervous system or to the cerebral spinal fluid." Neither Sanberg nor Weiss nor Uchida teaches the administration of cells to a plurality of sites in the central nervous system or cerebral spinal fluid. All of the references are directed to the administration of cells to the brain, not the entire central nervous system and not the cerebral spinal fluid. Also, as stated

above, none of the references teach the administration of about 6 million hNT cells. Given that the cited combination of references fails to teach each and every element of the claims in question, there can be no finding of obviousness. Claim 16 is dependent on claim 14 and is allowable as a matter of law upon the allowance of claim 14. For the foregoing reasons it is therefore respectfully requested that the rejection of claims 14 and 16 under 35 U.S.C. § 103(a) be withdrawn.

Sanberg fails to teach migration of cells and Weiss and Uchida fail to resolve that deficiency

Claim 15 is directed to "[a] method of improving sensory, motor or cognitive function in a person who has experienced brain damage due to a stroke which interferes with those functions, said method comprising delivering a sterile composition of at least 6 million hNT neuronal cells into a plurality of locations from which the hNT neuronal cells migrate to the damaged area." Neither Sanberg nor Weiss teach migration of cells to the damaged areas. Office uses the Uchida reference to overcome this deficiency, however Uchida is equivocal as to whether or not the cells migrate. (page 207) Office asserts that Uchida discounts the possibility of an alternative explanation for the movement of cells since "care was taken to minimize the possibility of disrupting brain structures." (Office Action dated June 5, 2009) This statement by Office does not discount the possibility of an alternative explanation for the movement of cells when taken in context with the remaining portion of the sentence in question. The entire sentence reads:

> "Although care was taken to minimize the possibility of disrupting brain structures by the needle track (a single dorsal approach) or by injection pressure (minimum pressure, depositing cells in the ventricle rather than parenchyma), **it cannot be ruled out that the distant cells were deposited at their sites during implantation**. **Further studies by monitoring temporal and spatial alterations in cell migration in vivo are required to determine whether the mobile behavior of neural plate-derived cells in vitro is displayed also in the adult CNS environment**." (emphasis added)

The fact that care was taken does not discount alternative explanations for movement. It is also noteworthy that the experiments in Uchida were conducted *in vitro* as opposed to *in vivo*. In fact, Uchida states that *in vivo* studies are needed to actually determine if there is mobile behavior involved. Given that the combination of Sanberg in view of Weiss and Uchida fails to

teach the element of migration as dictated in claim 15, in addition to the shortcomings of failing to teach administration of about 6 million hNT cells into a plurality of locations as discussed previously, the cited combination fails to render the present application obvious.

In conclusion, for the foregoing reasons, it is therefore respectfully requested that the Office withdraw the rejection of claims 7, 10, 12-17 and 19 under 35 U.S.C. § 103(a).

Dinsmore in view of Grabowski

Claims 20-28 and 30 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Dinsmore (US Patent 6,140,116) (hereinafter "Dinsmore") in view of Grabowski et al. (1994. Exp Neural. 127(1):126-136). Applicant respectfully traverses this rejection on the grounds that one or more elements are missing from the cited combination.

Independent claim 20 has been amended to include the limitation of administering about 6 million neuronal cells. As stated by Office on page 7 and 8 of the Office Action dated June 5, 2009, Dinsmore recites the administration of 12-20 million cells per subject. Dinsmore does not disclose the administration of less than 12 million cells and certainly does not disclose the administration of about 6 million neuronal cells for treatment of stroke. The administration of 12 million cells is twice the number of cells used in the present invention. MPEP §2143.02 requires that there must be a reasonable expectation of success in order for a finding of obviousness to be maintained. In the present case, the administration of half of the number of cells that were administered in Dinsmore did not have a reasonable expectation of success at the time of the invention.

Furthermore, Office uses Grabowski to overcome the deficiencies of Dinsmore with regard to the at least 3 hour delay for treatment in amended claim 20. The reasons why Grabowski fails to overcome this deficiency has been thoroughly discussed *supra* with respect to the rejection of claim 1. Given that the cited combination fails to teach every limitation of the claims, it cannot be said to obviate the present invention. Claims 22-28 and 30 depend from amended independent claim 20 and are allowable as a matter of law upon the allowance of claim 20. Applicant respectfully requests the withdrawal of the rejection as to claims 20-28 and 30.

Dinsmore in view of Grabowski in further view of Larazov-Spiegler

Claims 20-30 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Dinsmore (US Patent 6,140,116) (hereinafter "Dinsmore") in view of Grabowski et al. (1994. Exp Neural. 127(1):126-136) in further view of Larazov-Spiegler (FASEB, 1996, 10:1296-1302) (hereinafter "Larazov-Spiegler"). Applicant respectfully traverses this rejection on the grounds that one or more elements are missing from the cited combination.

Amended independent claim 20 discloses that administration of about 6 million neuronal cells for treatment of morbidity due to stroke. The deficiencies of the cited combination of Dinsmore and Grabowski with respect to the administration of about 6 million neuronal cells for the treatment of morbidity due to stroke have been discussed *supra*. Larazov-Spiegler fails to overcome these deficiencies. As such, the cited combination fails to teach each and every limitation of the claims and as such cannot be said to obviate the present invention. Claims 22-30 depend from independent claim 20 and are allowable as a matter of law upon the allowance of claim 20. Applicant respectfully requests that withdrawal of the rejection and the allowance of claims 20 and 22-30.

Conclusion

For the reasons cited above, Applicant believes that claims 1-2, 4, 7, 10, 12-17, 19-20, and 22-30 are patentable and in condition for allowance.

If the Office is not fully persuaded as to the merits of Applicant's position, or if an Examiner's Amendment would place the pending claims in condition for allowance, a telephone call to the undersigned at (813) 925-8505 is requested.

Very respectfully,

SMITH & HOPEN

By: /michele l lawson/

Dated: November 4, 2009

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CERTIFICATE OF ELECTRONIC TRANSMISSION
(37 C.F.R. 1.8(a))

I HEREBY CERTIFY that this Amendment F is being electronically transmitted to the United States Patent and Trademark Office through EFS Web on November 4, 2009.

Date: November 4, 2009

/lauren reeves/
Lauren Reeves